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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/410,462	10/01/1999	ANGELICA WILLIAMS		6889

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EXAMINER	
SORBELLO, ELEANOR	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 01/17/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/410,462	Applicant(s) WILLIAMS ET AL.	
	Examiner Eleanor Sorbello	Art Unit 1633	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Prosecution Application

1. The request filed on December 5, 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/410,462 is acceptable and a CPA has been established. An action on the CPA follows.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-24 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of substantially and selectively reducing tumor size by the intratumoral injection of Ad5 adenoviral vectors dl922/947 or dl1107 or pm 928, **does not** reasonably provide enablement for other limitations encompassed by the claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The unpredictable factors with regards to site of injection for in vivo applications wherein adenoviral vectors carrying specific deletions are administered, are discussed in Office actions dated 9/15/00 and 6/5/01 remain for reasons of record.

Therefore, in view of the state of the art, nature of the invention, breadth of the claims, one of skill in the art will require undue experimentation to make and use the invention in scope with claims.

Therefore, claims 1-24 remain rejected.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 6, 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 7 are rejected for being indefinite because the claims recite amino acid numbers, but the claims are not limited to the Ad5 although the specification refers to Ad5. If the claims are amended to indicate a particular sequence, the claims will require sequence compliance.

Claims 6, 7 are rejected for being indefinite because the claims recite specific amino acids of an E1A polypeptide, but do not specify which specific E1A polypeptide they are claiming. There are at least 3 polypeptides encoded by the E1A region.

Claims 6, 7 are rejected for being indefinite because the claims recite "mutation in the E1A-CR2 region" which is DNA and subsequently recite "deletion or substitution of one or more amino acids". The claim needs to be amended to recite that the E1A-CR2 region encodes an amino acid sequence comprising the deletion or substitution.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claims 21, 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamashita, T. et al. (Oncogene (1993), 8, 2433-2441).

Yamashita et al. teach adenovirus 5 E1A mutants (dl922/947) incapable of binding to RB. (See abstract, lines 31, 32). For the purpose of examination under 35 U.S.C. 102(b), these claims are being examined for features comprising the vector. The functional language of the claims drawn to pharmaceutical compositions, comprising the adenoviral mutant described above, does not lend any additional features to the vector, and is an "intended use". The composition has no other components other than the components of the adenovirus and a pharmaceutically acceptable carrier. Therefore, claims 21, 22 are rejected as being anticipated by Yamashia et al.

8. Claims 21, 23, 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Shisler, J, et al. (Journal of Virology, Jan. 1996, page 68-77).

Shisler et al. teach adenoviruses wherein the E1A region binds to RB. (see abstract and page 69, col. 1, lines 5-24, and Fig. 1). Shisler et al. teach adenoviral

mutants dl1107 and others with pm928. The pharmaceutical composition language of the claims do not lend any other feature to the product claim as discussed above. Therefore, claims 21, 23, 24 are rejected as being anticipated by Shisler et al.

9. Claims 1-6, 21, 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Bishoff et al. (U. S. Pat. NO: 6,080,5780.)

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Bishoff et al. teach methods of differentially selecting neoplastic cells from non-neoplastic cells by introducing an adenoviral construct comprising a deletion in the E1A region that lacks the CR2 domain capable of binding RB. Bishoff's novel constructs comprise a mutation such as a deletion or a point mutation in the CR2 domain (amino acids 120-139 in Ad 5). (see col. 10, paragraph 2). In some embodiments, a negative selectable gene such as an HSV tk gene is operably linked to an early region E2, E1a or E2b enhancer/promoter, wherein the negative selectable gene is preferentially transcribed in infected cells which express a replication phenotype ie. neoplastic cells and provides negative selection of such cells. (see col. 3, lines 66-67 and col. 4).

Therefore, claims 1-6, 21, 25 are rejected under 102(e) as being anticipated by Bishoff et al.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-10, 21-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bishoff in view of Yamashita, T. or Shisler et al.

Bishoff taught methods as discussed above under the 35 U.S.C. 102(e) rejection.

However, Bishoff et al. did not teach specific adenoviral mutants such as dl922/947 or dl1107 or pm928.

Yamashita et al. teach adenovirus 5 E1A mutants (dl922/947) incapable of binding to RB.

Shisler et al. teach adenoviruses wherein the E1A region binds to RB. (see abstract and page 69, col. 1, lines 5-24, and Fig. 1). Shisler et al. teach adenoviral mutants dl1107 and others with pm928.

However, because Bishoff's methods required an adenoviral mutant comprising a deletion or point mutation in the E1A binding region that prevents the binding of the RB protein, applicants would have been motivated to include the mutants taught by Yamashita and Shisler et al. in the instant invention.

Therefore, it would have been obvious to include the adenoviral constructs such as dl922/947, dl1107 and pm928 in methods of selectively killing dividing cells in a cell population of dividing cancerous cells and normal cells wherein RB protein is unable to bind the mutants of the instant invention, thereby resulting in the selection required.

Claims 1-10, 21-28 are rejected for being obvious.

12. Examiner reiterates that which was stated in the Final Office Action dated 6/5/01, wherein, applicants requested examiner to substitute new drawing sheets Figures 3C-4B, on sheets 5/7, 6/7 and 7/7, for the originally filed drawings. However, examiner does not see the difference between the new drawing sheets and the previously filed drawings. If differences exist, applicants were requested to point it out to examiner.

Conclusion

13. Claims 1-28 remain rejected.

14. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 *(http://www.uspto.gov)* and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED to facilitate further examination.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER